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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,664	10/08/1999	MICHAEL SUNDSTROM	10806-96	6767

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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/12/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/355,664	SUNDSTROM ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on September 03, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/355,664 is acceptable and a CPA has been established. An action on the CPA follows.

Response to Amendment

1. Claims 7-9 have been amended and claims 42-43 have been added as requested in the amendment of Paper No. 20, filed on September 03, 2002. Claims 1, 2, 4-10 and 42-43 are pending in the instant application.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on September 03, 2002 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

5. Claims 1, 2, 4-9 and 42-43 are rejected under 35 U.S.C. 112, first paragraph for reasons of record as applied to claim 19 in section 10 of Paper No. 10 and claims 1-2 and 4-9 in section 5 of Paper No.16. Briefly, the instant specification, while being enabling for a modified human growth hormone receptor (hGHR) consisting of residues 32-237 or 32-234 of the native hGHR

molecule, capable of being crystallized without being complexed to a ligand molecule, does not reasonably provide enablement for a cytokine receptor protein modified in the extracellular domain capable of being crystallized without being complexed to a ligand molecule.

The instant claims are directed to a cytokine receptor modified in the extracellular domain in a way that at least one molecular segment, which contributes to a disordered structure is deleted, such modified receptor being able to crystallize without being complexed to a ligand molecule. Note that when analyzing the enablement scope of the claims, the claims are to be given their broadest reasonable interpretation that is consistent with the specification and that the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. As such, the broadest reasonable interpretation of the invention of claims 1, 2, 4, 8 and 42-43 is a cytokine receptor protein in its full length, including all of the extracellular, transmembrane and intracellular domains, which is modified in the extracellular domain. The instant specification fails to provide any guidance as to how to generate crystals of a cytokine receptor, which is modified in the extracellular domain by deletion of a molecular segment, which contributes to a disordered structure. There is no evidence or sound scientific reasoning presented in the instant specification or found in the prior art that would support a conclusion that such crystallization of any cytokine receptor is possible or was ever achieved because all of the teachings of the instant specifications are directed to a very specific segment of only one example of a cytokine receptor, which is human growth hormone receptor $hGHR_{1-237}$.

The instant specification clearly indicates that so far all attempts to crystallize a native unliganded molecule of $hGHR_{1-237}$ have failed (page 7, third paragraph of the instant substitute

specification). It is further indicated that it was a surprising discovery, which led to the instant invention, that truncation of the extracellular domain of $hGHR_{1-237}$ and formation of truncated $hGHR_{32-237}$ resulted in easy crystallization, without binding to a ligand, of the modified molecule (page 7, last paragraph, see also page 4, first paragraph of the instant substitute specification). Thus, it is clear that modified extracellular domain of hGHR, $hGHR_{32-237}$ precisely, can be crystallized without being complexed to a ligand molecule. There is no indication in the instant specification or in the teachings of the prior art that would support a conclusion that similar modification of any cytokine receptor would enable one skilled in the art to create crystals of an unliganded molecule of such receptor.

Applicant argues that "it is well within the ability of one of ordinary skill in the art, and in fact easy, to determine parts of a cytokine receptor protein which contribute to a disordered structure for deletion according to the present invention" (page 4, second paragraph of the Response). Applicant further submits that "hGHR is well recognized in the art as representative of cytokine receptor proteins" (page 5, third paragraph). Various publications are quoted on page 5 to support this statement. This has not been found to be persuasive for the following reasons.

The fact that hGHR has structural homology to various cytokine receptors does not provide a basis for concluding that truncation of an extracellular domain of any cytokine receptor would enable its crystallization without being complexed to a ligand. As it has been mentioned earlier and also stated in the instant specification (see, for example, page 2, first paragraph of the instant substitute specification), the art of crystallization of cytokine receptors is very unpredictable. Therefore, one of ordinary skill in the art readily recognizes that in order to be able to practice the full scope of Applicant's invention, the adequate guidance must be supplied

by the specification. The instant specification fails to provide any guidance on how to modify any given disclosed or, as yet, undiscovered cytokine receptor protein, thus, urging an artisan to perform undue amount of experimentation in order to be able to practice the claimed invention.

Moreover, according to Applicant's own reasoning, the parts of the connecting regions, such as "small stretches of unordered amino acids with a high degree of motional freedom [...] are obviously not possible to remove from the soluble binding receptor while maintaining binding activity" (page 4, second paragraph of Response). Meanwhile, claim 1 encompasses deletion of any one "molecular segment which contributes to a disordered structure" (see claim 1). Therefore, one would reasonably conclude that there is not enough guidance provided in the instant specification to permit an artisan to predict which segments of a receptor protein contribute to a disordered structure, as would be needed to practice the claimed invention.

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. In the instant case, a skilled practitioner cannot rely upon one working example of successfully crystallized truncated extracellular domain of hGHR and reasonably expect that truncation of a molecular segment of any cytokine receptor protein, the segment that needs to be additionally identified, will allow equally successful yield of clear protein crystals. It would require undue experimentation and the making of a substantial inventive contribution for a skilled artisan to discover how to produce Applicants' invention as currently claimed.

6. Claims 1, 2, 6 and 8-10 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 is indefinite for reasons of record in section 7 of Paper No. 16. Applicant argues that the term "a molecule segment which contributes to a disordered structure" is definite and supported by the specification. However, apparently not every "molecule segment which contributes to a disordered structure" is suitable for deletion to achieve crystallization, see reasons of record in section 5 of the instant office action. Therefore, the recitation of "a molecule segment which contributes to a disordered structure" is considered vague and ambiguous.

8. Claims 8-10 are vague and indefinite for recitation of "a modified growth hormone receptor". It is not clear and cannot be determined form the claim what other possible modifications except truncation of C-terminal end are encompassed by the claim. Clarification is required.

Furthermore, although the full sequence of the human growth hormone receptor is well defined in the art, because the modifications of the claimed specific segment of hGHR are indefinite, in order to perform a sequence search for the claimed modified segment, Applicant is required to submit information regarding precise sequence of the claimed invention. Applicant needs to provide a computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or

1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

9. Claims 2 and 6 are indefinite for being dependent from the indefinite claims.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
November 7, 2002 OC

JOHN ULM
PRIMARY EXAMINER
GROUP 1600